


## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference KRKA2002/175	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/SI 03/00024	International filing date (day/month/year) 14.07.2003	Priority date (day/month/year) 15.07.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/551		
Applicant KRKA, D.D., NOVO MESTO et al.		

1.	This International preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	<p>This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of    sheets.</p>
3.	<p>This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the opinion</li> <li>II   <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V    <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul>

Date of submission of the demand  06.01.2004	Date of completion of this report  22.11.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Wolf, C  Telephone No. +49 89 2399-8285



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/SI 03/00024

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-19 as originally filed

**Claims, Numbers**

1-23 as originally filed

**Drawings, Figures**

1-6 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/SI 03/00024

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-23
	No: Claims	
Inventive step (IS)	Yes: Claims	1-17
	No: Claims	18-23
Industrial applicability (IA)	Yes: Claims	1-23
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/SI 03/00024

**re item V:**

The following documents are cited in the International Search Report:

- D1: WO 01/47933 A (WAIN CHRISTOPHER PAUL ;HAMIED YUSUF KHWAJA (IN); RAO DHARMARAJ RAM) 5 July 2001 (2001-07-05)
- D2: EP-A-0 733 634 (LILLY INDUSTRIES LTD ;LILLY CO ELI (US)) 25 September 1996 (1996-09-25)
- D3: EP-A-0 733 635 (LILLY INDUSTRIES LTD ;LILLY CO ELI (US)) 25 September 1996 (1996-09-25)
- D4: US-A-5 229 382 (CHAKRABARTI JIBAN KUMAR ET AL) 20 July 1993 (1993-07-20).

The processes for preparing olanzapine form I, specific solvates of olanzapine as starting material and the polymorph form (A) of olanzapine and its preparation process as claimed in present claims 1-23 appear to be novel in the light of D1-D4.

Technical problem underlying the present application was the provision of an alternative process for the preparation of form I of olanzapine.

As the Applicant submitted with his last letter the process as claimed is superior over the closest prior art process disclosed in D4 by using a solvent mixture containing 2-propanol. So this process and the new starting material appears to involve an inventive step over the prior art.

However, claims 18-23 which refer to a new polymorph A of olanzapine and the process for the preparation thereof appear to lack an inventive step.

The new polymorph A appears to have the same pharmacological effect as the other known polymorphs and the process for its preparation in claim 22 appears to be a common process (without the essential feature of 2-propanol) and has no reference back to the process of claim 1 where 2-propanol is involved on which the inventive step assessment of claims 1-17 has been based.

In the regional phase a non-unity objection could be made since claim 1-17 and claims 18-23 appear to correspond to two different technical problems (the essential feature of 2-propanol missing in the process for the preparation of polymorph A).